UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,811	05/04/2006	Philipp E. Scherer	21580YP	8553

210 7590 11/12/2009

MERCK AND CO., INC
P O BOX 2000
RAHWAY, NJ 07065-0907

EXAMINER	
RIDER, LANCE W	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
11/12/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,811	SCHERER ET AL.	
	Examiner	Art Unit	
	LANCE RIDER	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *22-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/04/2006 and 03/27/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1-33 are currently pending, claims 22-33 have been withdrawn due to the election requirement filed on August 3rd 2009.

Election/Restrictions

Applicant's election of Group I, claims 1-21, in the reply filed on August 31st 2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Information Disclosure Statement

The Information Disclosure Statement (IDS), filed by applicant on May 4th 2006, March 27th 2008, has been considered by the examiner in the present case.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hirose, H., et al., (Metabolism, 2002) in view of Tsao, T., et al., (Journal of Biological Chemistry, 2002), Hackeng, W.H.L., et al., (Journal of Clinical Endocrinology and Metabolism, 1986), Furuya, Y., et al, (International Journal of Urology, 2000), and Lemieux, I., et al., (Archives of Internal Medicine, 2001).

Hirose, H., et al., discloses a method for determining the effects of a drug on metabolic parameters in diabetic patients. The study shows the positive steps of

measuring the total concentration of the serum marker adiponectin in diabetic patients before a treatment. The patients were then treated with pioglitazone. Pioglitazone is a PPAR-gamma agonist with a TDZ structure meeting the limitations recited in instant claims 9-11. The patients total serum adiponectin levels were then measured 3 months after commencement of the pioglitazone treatment. It is also disclosed that adiponectin levels increased during treatment with the diabetes therapy pioglitazone, thus showing that an increase in total adiponectin levels correlate with a response to a diabetes therapy. (See page 315, paragraph 3, and page 316, figure 1.)

Hirose, H., et al., does not disclose the measurement of HMW adiponectin or its ratio to the total or LMW adiponectin levels.

Tsao, T., et al., discloses the measurement of HMW adiponectin (Acrp30) and that HWM adiponectin is the active version of adiponectin. It is reported in the abstract and throughout the disclosure that the HMW form of adiponectin and not the LMW form is responsible for the biological activity of adiponectin, specifically its function in the biological activation of NF-kB signaling. Tsao, T., et al., also indicates that the distribution (ie. ratio) of the HMW and LWM forms of adiponectin may be biologically important. (See page 29359, paragraph 3). Tsao, T., et al., indicates a reason for measuring just the HMW adiponectin levels, as HMW adiponectin is the biologically relevant species of adiponectin.

Tsao, T., et al., does not indicate measuring the ratio of HMW to total or LMW adiponectin for this particular disease marker.

Hackeng, W.H.L., et al., (Journal of Clinical Endocrinology and Metabolism, 1986), Furuya, Y., et al, (International Journal of Urology, 2000), and Lemieux, I., et al., (Archives of Internal Medicine, 2001) disclose methods for measuring important serum markers. Hackeng, W.H.L., et al., discloses the measurement of the ratio of intact to total parathyroid hormone as a measurement in diagnosis and treatment of parathyroid disorders. Hackeng, W.H.L., et al., specifically states that measuring both the "individual maker", intact parathyroid hormone and the total "class" of parathyroid hormone is more specific and sensitive than measuring the class of the marker alone. Furuya, Y., et al, (International Journal of Urology, 2000) disclose the measurement of free to total prostate specific antigen as a measurement in the diagnosis and treatment of prostate cancer. Lemieux, I., et al., (Archives of Internal Medicine, 2001) disclose the measurement of total cholesterol versus HDL cholesterol or LDL versus HDL cholesterol as a measurement in the diagnosis and treatment of heart disease. All of these references disclose the measurement of a ratio of the total amount of a disease marker to its active portion. By measuring the ratio of the total amount of the disease marker, "the class", to the active portion of the disease marker, "the individual", these studies show greater specificity and sensitivity than measuring just the class of the disease markers provides. It was therefore common practice for the skilled artisan at the time of the invention to measure ratios between the class and individuals of that class for many different disease markers.

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Hirose, H., et al., with the teachings of

Tsao, T., et al., and those of Hackeng, W.H.L., et al., Furuya, Y., et al., and Lemieux, I., et al.in order to provide an improved assay for diabetes (insulin resistance). Methods for determining the response of a patient to therapies for insulin resistance by measuring total adiponectin were known. It was also known that HMW adiponectin was the active species for this "class" of markers. As it was common practice in the art to measure ratios between the class of a disease marker and the biologically important individuals of that class, measuring the ratio between total adiponectin and its biologically important individual would have been obvious to the skilled artisan. In addition as Hackeng, W.H.L., et al., specifically teaches that measuring the ratios between the class and individuals of that class for disease markers increases the accuracy of such assays, the skilled artisan would have been further motivated to make this combination in order to improve the already known assay measuring total adiponectin.

The artisan would also have had a reasonable expectation of success since the assays for measuring both total and HMW adiponectin were already used for measuring serum adiponectin.

Clams 3-8, and 13-21 are drawn to a method in which the patient is determined to be a responder based upon the change in the HMW to the total adiponectin ratio at set time periods after treatment commences. Determining such a threshold where one determines a patient is a responder is a mental process. It was already known that an increase in total adiponectin correlated with a response to insulin treatment. As such the skilled artisan was already capable of determining when a patient was responding to treatments based upon changes in total adiponectin levels. Finding a corresponding

threshold for the ratio of HMW to total adiponectin would follow the same mental process. For those of ordinary skill in the art, such as diagnosticians, it was common practice to determine when patients were responding to a therapy. Such determinations are based upon many factors such as the age, weight, size, gender, and extenuating medical conditions present for each patient, all of which were common factors used in such diagnosis.

. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). In the instant case methods of measuring ratios of adiponectin levels and determining a patient's response to therapeutic treatment based on those levels were well known in the art at the time of the invention. The specific threshold of such ratios at which a patient was considered to be responsive to such a treatment were not specifically disclosed, but the determination of a threshold at which a patient was responding to a treatment would have common practice for those of skill in the art at the time of the invention.

Conclusion

No claims are currently allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LANCE RIDER whose telephone number is (571)270-1337. The examiner can normally be reached on M-F 11-12 and 1-4.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571)272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LANCE RIDER/
Examiner, Art Unit 1618

/Eric E Silverman/
Primary Examiner, Art Unit 1618